REMARKS/ARGUMENTS

Upon entry of this amendment, Claims 21, 25, 30-37, 39-46, and 50-52 are pending.

Claims 1-20, 22-24, and 26-29 were previously canceled. Claims 1 and 8-19 remain canceled without prejudice, as being drawn to non-elected subject matter. Claims 47-49 and 54 are hereby canceled, without prejudice, as falling within the withdrawn non-elected subject matter. Claims 38 and 53 are canceled.

Claims 21, 25 and 50 are amended by inserting "isolated" before polypeptide (specification pg. 6, line 6[1]), and by deleting the language "said polypeptide present in said composition in an amount effective to induce antibodies that recognize SEQ ID NO: 4 in a mammalian subject". Claims 21 and 25 are also amended by adding the language "whereby said polypeptide is isolatable from *Neisseria* bacteria" (specification pg. 11, line 29 – pg. 12, lines 1-11, 26-28; pg. 13, lines 10-12; pg. 18, line 28-pg. 19, line 11; and Examples 2 and 3). Claims 21 and 50 are further amended by adding "whereby said composition induces antibodies in a mammalian patient that bind to SEQ ID NO: 4 on the surface of said *Neisseria* bacteria and that interfere with the binding of said bacteria to mammalian cells" (pg. 20, lines 26-29; pg. 25, lines 25-30; pg. 26, line 14- pg. 27, line 2; pg. 35, lines 7-10; and in Example 8 at pg. 53). Note that the antiserum used in Example 8 was developed to the first 178 amino acids of SEQ ID NO: 2. The first 178 amino acids of SEQ ID NO: 2 differ from the first 178 amino acids of SEQ ID NO: 4 by only 3 amino acids. Thus the polypeptide used to immunize the mammalian subjects of the preceding examples falls within the claim language "an isolated polypeptide comprising at least eight consecutive amino acids from the amino acid sequence of SEQ ID NO: 4, which is isolatable from a *Neisseria* bacteria.

Claim 25 is further amended by deleting the term "detection system".

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[1] All recitations of specification pages cited are those of the 'clean copy' of the specification filed on June 26, 2003, which is a continuation of the parent application 09/177,319 and contained minor amendments to the Cross-reference and corrected spelling, typographical and grammatical errors in the parent application only, as well as a new claim set fully supported by the parent application.

Claims 34 and 44 are amended by clarifying that the proteins of the other *Neisseria* bacteria appear as reactive bands of approximately 85 kD on a Western blot (specification pg. 52, line 29 through pg. 53, line 7 and Fig. 6).

Claims 21, 25, 32, 34-37, 39, 42-44 and 51-52 are also amended in an effort to remove or replace claim language objected to by the examiner in the 35 USC §112 rejections stated below. Support for use of the word "bind" and "associated with" are found at pg. 30, lines 16-25. Support for the diagnostic reagent language of claim 25 is found at pg. 30, lines 9-19.

Applicants reserve the right to prosecute the non-elected claims and subject matter voluntarily removed from the pending claims in a divisional or continuation application filed during the pendency of the present application.

I. Double Patenting

Claims 21, 50, 30 and 31 are rejected under the judicially created doctrine of obviousness-type double patenting over claim 1 of US Patent No. 6,610,306.

In view of the attached submission of a terminal disclaimer, this ground for rejection is satisfied.

II. 35 USC §112, First Paragraph Rejection – New Matter

The examiner rejects pending claims 21, 25, 30-46, and 50-53 for allegedly containing subject matter not described in the specification, i.e., new matter, in the pages of the Office Action spanning 6-13. The examiner states that new matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method.

Applicants respectfully request reconsideration and withdrawal of these grounds for rejection in view of the above amendment, the support for the amendments recited herein, the support cited in the preceding response to the last Office Action, and the following remarks. In view of the length of the rejection under this paragraph and

recitation of a considerable portion of the pending claim language, Applicants has, for brevity, simply referred to this rejection as a whole.

The Examiner appears to reject the newly introduced claim language because the language is not present *in haec verba* in the specification. However, as clearly stated by the MPEP§2163, newly added claim limitations can be *implicitly or inherently* supported in the specification as well as by express disclosure. Also, MPEP §2163 at pg. 2100-183, col. 2 provides that to establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference and that it would *be so recognized by persons or ordinary skill* (emphasis added). The fundamental factual inquiry for any written description rejection is whether the specification conveys *with reasonable clarity* to those skilled in the art, that, as of the filing date sought, applicant was in possession of the invention as now claimed.

In making this new matter rejection based on amendments to the claims, the examiner is required to explain why one of skill in the art would not understand the disclosure to support the claims. It is not a sufficient establishment of new matter for the examiner to merely state that certain claim language is not *explicitly* used in the specification. As required by MPEP§2163 at pg. 2100-176, col. 2, the examiner must provide present *evidence or reasoning* ***why*** *a person of skill in the art* would not recognize in the disclosure a description of the invention defined by the claims. With respect, Applicants submit that the examiner has not provided such reasoning.

Applicants submit that this disclosure conveys *with reasonable clarity* to those skilled in the art, that, as of the filing date sought, Applicants were in possession of the invention of all pending claims. In summary, and as specified in the preceding response, Applicants' original specification clearly identifies SEQ ID NO: 2 and SEQ ID NO: 4 as homologous "OMP85" proteins having distinct structural similarities as well as having the ability to induce antibodies that are capable of recognizing a number of *Neisserial* OMP85 proteins. The term OMP85 is clearly used to refer to both SEQ ID NO: 2 and SEQ ID NO: 4. See, e.g., pg. 11, line 20- pg. 12, line 10 and the comparison of the sequences in Fig. 5. The specification points to the similarities among the protein

sequences (see pg. 16, lines 6-20), and the fact that the OMP85 *antigens* may be obtained as intact proteins, polypeptides or fragments, that such fragments may be as small as 5-8 consecutive amino acid sequences, and that such antigens or fragments share a biological activity, i.e., the ability to induce antibodies (pg. 18, line 27-pg. 21, line 4; pg. 25, line 14-15.) That the OMP85 polypeptides and fragments can induce antibodies is taught at pg. 26, line 13 et seq. That such OMP polypeptides and fragments can be used diagnostically is described at pgs. 29-33. That the OMP85 antigens and fragments, which can be immunogenic fragments (see pg. 35, line 20) can be used in compositions with pharmaceutical carriers is taught at pgs. 33-37 The specification teaches that these proteins or fragments may be fused to other polypeptides by conventional means (pg. 21, line 25-pg. 22, line 27).

Finally, the examples provide evidence that an illustrative antibody induced by an OMP85 protein fragment of amino acids 1-178 of SEQ ID NO: 2 which is virtually identical to the same sequence in SEQ ID NO: 4, but for 3 amino acids (see FIG. 5) induces antibodies that recognize or bind with the **both** OMP85 of SEQ ID NO: 2 and SEQ ID NO: 4. The specification clearly teaches that antibodies induced by an OMP85 antigen of this invention recognized the OMP85 protein in multiple *Neisseria* strains, i.e., from six representative strains of *N. gonorrhoeae* and four strains of *N. meningitidis*. See, pg. 48, lines 1-8 and FIG. 3. See, also, Example 7, at pgs. 50-52 and accompanying FIGs. 6, 7A and 7B. These examples clearly demonstrate that the OMP85 antigen can induce antibodies capable of binding the OMP85 proteins of multiple *Neisseria* strains, but ***not*** in the tested strains of *Klebsiella, Pseudomonas, Salmonella, Shigella* and *E. coli*. See pg. 52, last line through pg. 53, line 2. Example 8 at pg. 53 also teaches that the antibodies induced by the OMP85 polypeptide bind to the surface of bacteria and interfere with the ability of the bacteria to adhere to the epithelial cells.

Given the entirety of the specification and the understanding of the skilled artisan, it is respectfully submitted that all language used in independent claims 21, 25 and 50 are understood by one of skill in the art as supported at least implicitly or inherently, if not

explicitly, by the specification as filed.[2] As one example, one of skill in the art would understand that the identification of an "approximately 85kD" protein by identification on a Western blot is sufficiently clear for purposes of claims 34 and 44 to describe antibody binding. As another example, given the similarities of the sequences of SEQ ID NO: 2 and SEQ ID NO: 4 overall, as well as structural similarities of the OMP85 proteins, and the relative identity of the exemplified sequence used in the examples, one of skill in the art would understand that the signal sequence identified in FIG. 2 for SEQ ID NO: 2 is identical and in the identical position in the homologous OMP85 protein of SEQ ID NO: 4. Thus, the identification of that signal sequence and cleavage site in SEQ ID NO: 2 is inherent for the same sequence and cleavage site in SEQ ID NO: 4. One of skill in the art, given the present disclosure, would find inherent support for the claim language of claims 43 and 51. Similarly, given the description of the two OMP85 proteins, one of skill in the art would understand from the specification that a polypeptide comprising at least eight consecutive amino acids of SEQ ID NO:4 which is isolatable from *Neisseria* bacteria describes both antigenic fragments and the intact proteins of the two homologs which are 95% identical in sequence, i.e., SEQ ID NO: 4 and SEQ ID NO: 2.

Given the entirety of the specification, the preceding response which identified the supporting portions of the specification, and the understanding of the skilled artisan, it is respectfully submitted that none of the pending, rejected claims introduce new matter. In view of the amended language of the claims, and the clear support of the application for language currently employed in the claims, Applicants respectfully request that the examiner reconsider and withdraw this rejection as against any of the claims now pending.

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[2] Even if every nuance of the claims is not explicitly described in the specification, the critical issue is the understanding of the skilled artisan. See, e.g., Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991).

III. 35 USC §112, Second Paragraph - Indefiniteness

Claims 21, 25, 30-46 and 50-53 are rejected as allegedly being indefinite.

Applicants respectfully request reconsideration and withdrawal of these grounds for rejection in view of the amendment of the claims.

Claims 38 and 53 are canceled.

Claims 21, 37, 39, 43 and 50-52 now have "said" before the recitations of "SEQ ID NO: 4", thereby satisfying that specific ground for rejection.

Claim 25 has been amended to describe the polypeptide and remove the language relating to inducing antibodies. See, the description of the polypeptide and fragments at pgs. 19-21 and the diagnostic compositions described at pg. 30, lines 9-19. This amendment is believed to satisfy this rejection.

Claims 32-26, 42 and 44 are amended to replace "*Neisseriae*" with "*Neisseria*" as suggested by the examiner and insert "*Neisseria*" before *meningitidis*.

The rejection of the term "associated with" in claims 25 and 39 is hereby traversed. It is respectfully submitted that one of skill in the art is aware of the many different ways in which one would associate a label, whether it be a fluorescent protein, a radioactive label, another antibody, or any other conventional signal generating label commonly used in diagnostic assays with a protein diagnostic reagent. Applicants do not have the obligation to teach the person of skill in the art those techniques which would be obvious or readily attainable from conventional textbooks. Thus, Applicants submit that the term associated with as used in the specification is sufficient to teach one of skill in the art how to make a diagnostic reagent of the sequences disclosed in this specification. Applicants respectfully request withdrawal of this ground for rejection.

The reference to "approximately 85kD" was clarified in claims 34 and 44 by referring to its detection in a Western blot, which is believed to be clear to one of skill in the art.

The amendment to claims 34 and 44 obviated the need for an amendment in claims 35 and 45.

Claim 52 was amended to insert "said" before "polypeptide".

The above amendments are believed to satisfy and permit withdrawal of these grounds for rejection of all pending claims.

IV. 35 USC §102(a) Rejection

Claims 21, 25, 30-36, 39-42, 44-46, 50 and 52 are rejected as allegedly anticipated by Wetzler et al, 1989 J. Exp. Med. 169:2199-2210 as evidenced by US 5,554,372 (Hunter) or US 20040033234 (Berinstein) and Harlow et al, in Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, NY, pp.471-510 (1988).

Wexler refers to a composition comprising N. gonorrhoeae whole cells lysates showing a protein band at MW of approximately 85,000 and is expected to inherently and necessarily comprise the instantly recited polypeptide comprising at least 8 consecutive amino acids from SEQ ID NO: 4

Applicants respectfully submit that this rejection may be withdrawn based on the amendment of claims 21, 25 and 50 to provide that the compositions contain *isolated* polypeptides. Such isolated polypeptides cannot be anticipated by a description of a cell lysate.

V. 35 USC §102(e)(2) Rejection

Claims 21, 25 and 30-46 are rejected as allegedly anticipated by US 6,551,795 (Rubenfield). Rubenfield discloses an isolated or substantially pure P. aeruginosa 648 amino acid polypeptide having an amino acid sequence comprising the eight consecutive amino acids VRVETADG which are identical to an 8-mer of the instant SEQ ID NO: 4. Rubenfield's polypeptide is employed in a vaccine composition, a diagnostic composition, a diagnostic reagent, a kit, etc.

Applicants respectfully request reconsideration and withdrawal of this rejection. Independent claims 21 and 25 (and thus all claims 30-46 dependent therefrom) are amended to provide that the compositions contain a polypeptide that not only contains *at least* 8 consecutive amino acids of SEQ ID NO: 4, but that it must also be isolatable from ***Neisseria*** bacteria, which distinguishes the claims from Rubenfield's polypeptide which is **not** isolatable from *Neisseria*, but from *Pseudomonas*. Further, the composition of claim 21 is amended to provide that the composition not only contains a polypeptide isolatable from *Neisseria* bacteria, but that such polypeptide in the composition also

induces antibodies in a mammalian patient that bind to said amino acid sequence of SEQ ID NO: 4 on the surface of said *Neisseria* bacteria and that interfere with the ability of said *Neisseria* bacteria to adhere to mammalian cells.

Both the structural and functional requirements of the compositions of Claims 21 and 25 differ from the disclosure of Rubenfield. While the examiner indicates that Rubenfield's patent contains a SEQ ID NO: 24628 that comprises a sequence of 8 consecutive amino acids, which 8 amino acids duplicate the sequence of aa74-81 of Applicants' SEQ ID NO: 4, nothing in Rubenfield teaches or discloses that said SEQ ID NO: 24628 meets the other requirements of Applicants' amended claim 21. In fact, Rubenfield ***teaches away*** from Applicants' claims in Rubenfield's assertions that its intent is to obtain "bacterial specific" compositions and methods (col. 2, lines 17-23) for *P. aeruginosa* vaccines and diagnostics, in its definition of its polypeptides as having *P. aeruginosa* biological activity as having one to three of the properties listed in col. 13, lines 1-11, i.e., when expressed in the course of *P. aeruginosa* infection, the polypeptide promotes or mediates attachment of *P. aeruginosa* to a cell; it has enzymatic activity, structural or regulatory function characteristic of a *P. aeruginosa* protein, or the gene which encodes it can rescue a lethal mutation in a *P. aeruginosa* gene.

Rubenfield's extensive 908 column patent disclosure containing these above-referenced statements includes a tabular listing of over 20,000 different *P. aeruginosa* ORF sequence. None of these sequences are taught to have similarity to any *Neisserial* species. The mere occurrence of an 8 amino acid similarity in one of over 20,000 sequences does not teach or suggest to one of skill in the art the compositions of claims 21 or 25. Applicants submit that the mere occurrence of a duplicate 8 mer embedded in one of over 20,000 sequences from a different microorganism referenced in Rubenfield is not a sufficient disclosure to teach the polypeptides described in Applicants' claims 21 and 25. To provide an "enabling disclosure" sufficient to anticipate Applicants' claims, Rubenfield must be interpreted to place the public in possession of Applicants' claimed invention before the date of Applicants' invention (see MPEP §2121.01). Even with Rubenfield's disclosure of SEQ ID NO: 24628, a *P. aeruginosa* polypeptide, Applicants

fail to see how one of skill in the art would have been able to use that piece of information to create Applicants' compositions of claims 21 and 25.

Applicants respectfully request reconsideration and withdrawal of this rejection as against any pending claim.

VI. 35 USC §102(a) Rejection

Claims 21, 25, 31-36, 38-42, 44-46 50, 52, and 53 are allegedly anticipated by Manning et al, Microb. Pathogen., 25:11-22 (1998), using Richarme et al, Ann. Microbiol. 133A:199204 (1982) to show that every element of the claimed subject matter is disclosed by Manning. The examiner applies this rejection, asserting that Applicants' pending claims are not entitled to their priority date and are permitted only the date of June 26, 2003.

As argued above, the pending claims do not introduce new matter but are fully supported by the pending specification. The pending specification is a continuation of the prior application filed October 22, 1998 and has the same specification with minor formal and grammatical corrections. Therefore, this rejection cannot stand and the previously filed *In re Katz* declaration moots this rejection.

In view of the above amendments and remarks, Applicants respectfully request that the amended claims be permitted to issue in due course.

The Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or during the pendency of this application, or credit any overpayment in any fees to our Deposit Account Number 08-3040.

Respectfully submitted,
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